Why do oVEMPs become larger when you look up? Explaining the effect of gaze elevation on the ocular vestibular evoked myogenic potential

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Abstract: OBJECTIVES: The ocular vestibular evoked myogenic potential (oVEMP) is a vestibular reflex recorded from the inferior oblique (IO) muscles, which increases in amplitude during eye elevation. We investigated whether this effect of gaze elevation could be explained by movement of the IO closer to the recording electrode. METHODS: We compared oVEMPs recorded with different gaze elevations to those recorded with constant gaze position but electrodes placed at increasing distance from the eyes. oVEMPs were recorded in ten healthy subjects using bursts of skull vibration. RESULTS: oVEMP amplitude decreased more with decreasing gaze elevation (9 V from 24° up to neutral) than with increasing electrode distance (2.7 V from baseline to 6.4mm; P<0.005). The oVEMP recorded with gaze 24° down had delayed latency (by 4.5ms). CONCLUSION: The effect of gaze elevation on the oVEMP cannot be explained by changes in position of the muscle alone and is likely mainly due to increased tonic contraction of the IO muscle in up-gaze. The oVEMP recorded in down-gaze (when the IO is inactivated, but the IR activated) likely originates in the adjacent IR muscle. SIGNIFICANCE: Our results suggest that oVEMP amplitudes in extraocular muscles scale in response to changing tonic muscle activity.

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Why do oVEMPs become larger when you look up?
Explaining the effect of gaze elevation on the ocular vestibular evoked myogenic potential

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Running title: The effect of gaze on oVEMPs

Key words: oVEMP, gaze, vestibulo-ocular reflex, otolith, inferior oblique muscle

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Highlights:

- Gaze elevation significantly increases oVEMP amplitude, while gaze depression decreases amplitude and prolongs latency.
- This gaze effect is primarily due to changes in tonic eye muscle activity, while the contribution of changes in muscle-electrode distance is significant but small.
- oVEMPs recorded from below the eyes originate mainly in the inferior oblique muscle during up-gaze and in the inferior rectus muscle during down-gaze.

Abstract

Objectives: The ocular vestibular evoked myogenic potential (oVEMP) is a vestibular reflex recorded from the inferior oblique (IO) muscles, which increases in amplitude during eye elevation. We investigated whether this effect of gaze elevation could be explained by movement of the IO closer to the recording electrode.

Methods: We compared oVEMPs recorded with different gaze elevations to those recorded with constant gaze position but electrodes placed at increasing distance from the eyes. oVEMPs were recorded in ten healthy subjects using bursts of skull vibration.

Results: oVEMP amplitude decreased more with decreasing gaze elevation (9 μV from 24º up to neutral) than with increasing electrode distance (2.7 μV from baseline to 6.4 mm; P<0.005). The oVEMP recorded with gaze 24º down had delayed latency (by 4.5 ms).

Conclusion: The effect of gaze elevation on the oVEMP cannot be explained by changes in position of the muscle alone and is likely mainly due to increased tonic contraction of the IO muscle in up-gaze. The oVEMP recorded in down-gaze (when the IO is inactivated, but the IR activated) likely originates in the adjacent IR muscle.

Significance: Our results suggest that oVEMP amplitudes in extraocular muscles scale in response to changing tonic muscle activity.

Introduction

The ocular vestibular evoked myogenic potential (oVEMP) is a recently-described, vestibular-dependent reflex recorded from the extraocular muscles in humans (see Rosengren et al., 2010 for review). It is elicited by vestibular stimulation with vibration or loud sounds and is recorded from surface electrodes placed near the eyes. The oVEMP is part of the vestibulo-ocular reflex (VOR), as it represents the muscle activity that underlies a vestibular-evoked eye movement: it is, however, independent of the electrical activity generated by the corneoretinal dipole of the eye (i.e. the electro-oculogram, EOG; Todd et al., 2007; Welgampola et al., 2009). The reflex is best measured during up-gaze from electrodes placed below the eyes, as it is largest and most consistent under these conditions (e.g. Iwasaki et al., 2009; Rosengren et al., 2005). When thus measured, the oVEMP consists of a series of waves, beginning with a negativity which peaks at around 10 ms (n10). This potential is a ‘crossed’ reflex, i.e. recorded in the eye contralateral to the stimulated ear (Iwasaki et al., 2007), and is thought to be mediated by otolith fibres, as animal studies have shown that otolith afferents are preferentially activated by vibration and sound (Curthoys et al., 2006; Murofushi et al., 1997). As the n10 component of the reflex is abolished in patients with vestibular loss, the oVEMP has been introduced as a clinical test of otolith function.

Although many extraocular muscles may be activated by otolith stimulation, when recorded from beneath the eyes, the n10 response appears to originate in the inferior oblique (IO) muscle. We recently investigated the myogenic origin of the oVEMP by recording the motor unit activity of the extraocular muscles located closest to the recording site: the IO and inferior rectus (IR) muscles (Weber et al., 2012). The results showed a series of increases and decreases of IO motor unit discharge, beginning with an excitation of the muscle at approximately 10 ms. The IR was also excited, but the first peak of activity occurred later at about 15 ms. This demonstrated that, although both muscles are activated by the oVEMP stimulus, the n10 potential originates in the IO muscle and is excitatory, as predicted from its surface polarity (Colebatch and Rothwell, 2004).

An important property of the oVEMP is that its amplitude increases with up-gaze and decreases with down-gaze (Govender et al., 2009). Two hypotheses have been proposed to explain this: the first attributes the change in amplitude to movement of the IO muscle belly relative to the recording electrodes, while the second attributes the effect to changes in tonic activation of the IO at different vertical gaze angles (e.g. Chou et al., 2009; Govender et al., 2009; Huang et al., 2012; Iwasaki et al., 2008; Rosengren et al., 2005; Welgampola et al., 2009). The size of any potential can be expected to increase as the distance between the source and the electrodes is decreased. On the other hand, tonic activity of the muscle is an important contributor to the amplitude of the cervical VEMP (cVEMP), a similar (but inhibitory) short-latency vestibular reflex measured from the neck muscles (Colebatch et al., 1994; Lim et al., 1995). As the main actions of the IO are extorsion and elevation, the IO is activated during up-gaze. However, the demands on the VOR are different to those on postural muscles, and it is not clear whether reflexes elicited in the extraocular muscles can be expected to share the same properties.

As Demer et al. (2003) have measured the actual displacement of the IO muscle during changes in vertical gaze, it is possible to use this information to estimate the effect of muscle displacement relative to the recording electrodes. They used magnetic resonance imaging to compare the antero-posterior position of the IO at the point where it crosses the inferior rectus muscle during different levels of vertical gaze. Since the IO is maximally activated in up-gaze with adduction and inhibited in down-gaze with abduction, Demer et al. (2003) recorded the eyes in these positions as well as in neutral position. As the eye rotated from the down-gaze to the up-gaze position, the IO muscle belly moved 4.3 mm anteriorly with little change in vertical position. In the current study, we used the same gaze positions as Demer et al. (2003) to modulate oVEMP amplitude. We then simulated a 4.3 mm muscle displacement by systematically moving the recording electrodes away from the muscle while holding gaze (and therefore muscle position and activity) constant. If muscle displacement principally determined the gaze effect, we would expect to see a similar decrement in oVEMP amplitude with increasing electrode distance as occurs with the corresponding decreased gaze angle. Conversely, if muscle activity were more important, we would expect a greater modulation with vertical gaze change than with electrode displacement.

Methods

Subjects

Ten normal volunteers, with no history of vestibular or neurological disease, participated (3 female, 7 males; age range 26 to 48 years). The participants gave written informed consent according to the Declaration of Helsinki and the study was approved by the local ethics committee (Kantonale Ethik-Kommission Zurich, 2010-0177/3).

Stimulation and recording parameters

The oVEMP stimulus was a 500 Hz, 4 ms burst of vibration delivered with a hand-held minishaker positioned over the hairline near Fz (i.e. an unshaped sinusoid, delivered at approximately 148 dB force level (FL) peak; minishaker model 4810; amplifier model 2706, Brüel & Kjaer P/L, Denmark). This stimulus produces a predominant interaural (outwards) head acceleration with initial peak amplitude typically of 0.1 g (Weber et al., 2012). The stimuli were generated with customized software using a laboratory interface (micro1401, Cambridge Electronic Design (CED), Cambridge, UK) and delivered at a rate of 7.5 Hz for 200 repetitions per trial. A guide point was marked on the forehead to ensure that the stimulus was applied to the same point in each trial (Figure 1B). We recorded surface potentials from two recording electrodes and used a linked earlobe reference (Figure 1B). An earth electrode was placed on the left temple. The superior edge of the upper recording electrode was always aligned with one of several guide lines drawn underneath the eye and the lower recording electrode was placed directly below it on the cheek (similar to a regular oVEMP montage). We reconstructed the typical bipolar electrode montage from this referential montage by subtracting the lower electrode trace from the upper electrode trace offline.

Surface EMG was recorded from the electrodes (Blue sensor N, Ambu, Ballerup, Denmark) with the same micro1401 data acquisition interface and custom software as described above. Data were sampled at 10 kHz for 70 ms (from 10 ms before to 60 ms following stimulus onset), amplified and bandpass filtered (5 Hz to 2 kHz). Negative potentials at the active electrodes were displayed as upward deflections.

Experiment design

Guidelines were drawn on the face below the left eye at the superior edge of the infraorbital margin (0 mm, baseline position) and 2.4, 6.2, 10, and 20 mm below this point. By moving the electrodes 2.4 or 6.2 mm away from the eyes, we created a displacement effect equivalent to the 4.3 mm gaze-evoked antero-posterior IO muscle movement measured by Demer et al. (2003). The values 2.4 and 6.2 mm were calculated based on the distances from the anterior edge of the IO muscle to the midpoint and superior edge of the recording electrode, respectively. We used these electrode regions to account for both the best recording area (the middle of the electrode) and the closest part of the electrode to the muscle (the superior edge of the electrode). The calculation of these values is outlined in Appendix A. We used the 10 and 20 mm positions to extend our range of measurement.

The experiment consisted of 2 blocks. In the first block, the electrodes were fixed in the baseline (0 mm) position and gaze angle was changed. Subjects sat in an adjustable chair at a distance of 1 m from a target board. They directed their gaze towards targets in the gaze up (24° elevation with 13° adduction), gaze neutral (0°, i.e. aligned with the left eye) and gaze down directions (24° depression with 5° abduction) (Figure 1A). These gaze angles matched those used by Demer et al. (2003) to measure IO displacement. Ocular VEMPs were recorded once at each gaze angle. In the second block, we tested the effect of electrode position. Gaze was fixed in the gaze up position (24° elevation with 13° adduction) and oVEMPs were measured from electrodes at each of the marked electrode positions (0, 2.4, 6.2, 10, and 20 mm). The electrodes were removed and reattached between each trial such that the upper edge of the primary recording electrode was aligned with the appropriate guideline. The order of the blocks and the order of trials within each block were counterbalanced to prevent order effects.

Data Analysis

Amplitudes were measured at the first negative (n10) and positive (p15) peaks and added to give peak-to-peak amplitude. Latencies were measured at the n10 peak and adjusted to correct for a 0.5 ms delay in the recording system. In the case of absent responses, amplitudes were assigned the value of 0 μV and latencies were omitted from analysis. Differences in oVEMP amplitude across conditions were examined with repeated-measures ANOVA and post hoc t-tests. Differences in latency were tested using non-parametric statistics (i.e. Friedman's two-way ANOVA by ranks and the Wilcoxon signed ranks test for related samples), as there were absent responses in some conditions. Values are reported in the text as mean ± standard deviation for amplitude and median (with the range in parentheses) for latency.

Results

We analysed the responses from the upper recording electrode in the referential montage to maximise the reliability of measurements in individual subjects. The responses recorded using the referential and bipolar electrode montages were very similar, but the referential montage produced responses approximately twice as large (Figure 2).

Gaze effect

Ocular VEMPs were present in all subjects when measured during up-gaze with the electrodes in the baseline position (Figure 2) and had a mean amplitude of 12.1 ± 8.8 μV and a median latency of 8.6 ms (range 8.0-11.5 ms). With progressive down-gaze there was a significant overall decline in oVEMP amplitude ($F_{(2,18)} = 11.6$, $P = 0.001$). In the neutral position, oVEMPs were absent in 3 out of 10 subjects and the mean amplitude decreased to 3.1 μV at 9.3 ms, about a quarter of the amplitude recorded during up-gaze ($t_{(9)} = 4.2$, $P = 0.002$). During down-gaze, the n10 oVEMP peak at about 10 ms was absent in all subjects. However, we recorded a later negative peak, with a mean amplitude of 5.8 μV and a median latency of 13.4 (range 11.2-15.4 ms; $Fr_{(2)} = 11.1$, $P = 0.004$). The latency of the peak recorded with down-gaze was significantly longer than the latencies recorded with up- or neutral-gaze ($W = 55$ and 28, $P = 0.005$ and 0.018), which were similar to each other ($W = 19.5$, $P = 0.352$). As seen from Figure 2B, the first negative peak with gaze down occurred at the same time as the positive p15 peak recorded with gaze up ($W = 25.5$, $P = 0.293$). The responses recorded with gaze neutral appeared to be a combination of those recorded with gaze up and down, both in the grand mean trace (Figure 2A), seen as a notch (marked *), and in individual traces, where two clear negative peaks were sometimes seen.

Electrode position effect

As illustrated in Figure 3, oVEMP amplitude also decreased significantly with increasing distance of the electrode from the eye ($F_{(4,32)} = 9.1$, $P < 0.001$), but there was no change in n10 latency ($Fr = 6.6$, $P = 0.157$). The amplitude of the oVEMP measured in the baseline position was 10.8 ± 9.7 μV, similar to the amplitude recorded under the same conditions when testing the effect of gaze ($t_{(9)} = 0.7$, $P = 0.499$). This amplitude decreased to 8.6 ± 8.2 and 8.1 ± 7.9 μV at the 2.4 and 6.2 mm electrode positions and to 3.7 ± 5.2 μV when measured 20 mm below baseline position. The reduction of amplitude over distance followed an exponential pattern ($y = 29.103e^{-0.0581x}$, $R^2 = 0.94$) and is illustrated in Figure 4. The exponential fit was superior to a linear one ($y = -0.37x + 16.61$, $R^2 = 0.89$). The decrement in amplitude between the baseline and 2.4 and 6.2 mm positions (mean 2.2 and 2.7 μV respectively, corresponding to decreases of 20 and 25%) was significantly smaller than the mean 9 μV (74%) decrease between the gaze up and neutral conditions ($t_{(9)} = 3.7$ and 3.3, $P =$ 0.005 and 0.009), demonstrating that the effect of gaze was significantly greater than the effect of electrode position.

Discussion

Our results clearly demonstrate that the effect of vertical gaze on the oVEMP is not primarily due to displacement of the IO muscle. Instead, the majority of the effect is likely due to tonic activity of the IO muscle. The IO has been shown to move anteriorly as the eyes move upwards (Demer et al., 2003), bringing the source of the signal closer to the recording electrodes. However, this movement is small and myogenic potentials are known to spread widely over the scalp (e.g. Thickbroom and Mastaglia, 1985). Our results demonstrate that, although there was a significant effect of muscle-electrode distance, displacement of the IO could not account for the majority of the gaze effect. The signal decrement caused by moving the electrodes was small (20-25%) compared to the decrement produced by depression of the eye from the gaze up to the gaze neutral (74%) and gaze down positions (100%, at 10 ms). This was the case whether one considered the distance of the muscle to the midpoint of the electrode or the closest point. Given the large size of this effect, minor inaccuracies in our estimate of the position of the IO relative to the orbit and electrodes are unlikely to have confounded our results.

The effect of vertical gaze direction on the oVEMP also extended beyond the amplitude of the reflex. During down-gaze, there was no response at 10 ms, but a negative peak occurred approximately 4.5 ms later. Govender et al. (2009) also reported a latency change of comparable size with maximal down-gaze. Such a large latency difference suggests that the initial oVEMP peak measured during down-gaze has a different origin to that recorded during up-gaze. There is strong evidence that this origin is the IR muscle, for two reasons: First, the latency difference between oVEMPs recorded in up- versus down-gaze is very similar to the latency difference recorded in the IO versus IR muscles during single motor unit recordings (Weber et al., 2012). In this report we recorded an excitation in both muscles, delayed by about 5 ms in the IR compared to the IO muscle. The latency and polarity of the oVEMP recorded in up-gaze matches that of the IO motor unit response, while the oVEMP recorded in down-gaze closely resembles the IR motor unit response. Second, our current results suggest that the tonic activity of the extraocular muscles is an important determinant of oVEMP amplitude. As the IR is activated by down-gaze, it is therefore likely that the oVEMP recorded during down-gaze originates in this muscle.

A combination of the factors 'tonic muscle activity' and 'proximity to electrode' is likely to explain the basic morphology of oVEMPs under most gaze and recording conditions, assuming that other factors are constant (such as the neural reflex input to the muscle). The IO dominates the surface potential during up-gaze as it is highly activated in this position and is the closest muscle to the electrode. The bellies of the next closest muscles - the inferior (IR) and lateral recti (LR) - are located much further back in the orbit (Kaufmann and Steffen, 2004) and these muscles are either tonically inhibited (IR) or only moderately activated (LR) by up-gaze. A similar argument can also be made for the IR muscle in down-gaze. Although the strength of the motor unit response of the IR and IO muscles to our stimulus appears to be similar (Weber et al., 2012), the more posterior location of the IR belly in the orbit means that any signal from the IR muscle belly is likely to be smaller when it reaches the surface, even when the muscle is tonically activated (which causes the IR belly to move even deeper into the orbit). The IR muscle has a length of approximately 37 mm, behind a tendon with length of 4.7 mm, meaning that the bulk of the muscle belly lies deep in the orbit (Kaufmann and Steffen, 2004). If we assume that the bulk of the IR muscle belly lies at least 15 mm posterior to the anterior edge of the IO muscle during down-gaze (i.e. equivalent to approximately 29.4 mm from the recording electrode), we can use the decay function from Figure 4 (reduction of oVEMP amplitude with increasing electrode distance) to estimate the size of the oVEMP expected at the surface. Using this value, the predicted size would be 5.3 μV, similar to the measured value of 5.8 μV of the oVEMP in down-gaze. Although the IO is closer to the electrodes, it is inactivated by down-gaze, and therefore does not appear to influence the down-gaze recording (although some cancellation of the IO and IR responses may occur as they are phase-shifted). In support of this model, the responses recorded with neutral-gaze appear to be a combination of the up- and down-gaze recordings and probably contain signals from both muscles (Figure 2). In this position, the IO and IR both have a moderate level of tonic activity, and addition of the signals from the two muscles (and possibly the lateral recti) would be expected, as the surface response is a summation of the electrical activity from all nearby sources (Keenan et al., 2005). A similar summation effect with neutral gaze was previously proposed by Todd et al. (2008), who used different vestibular stimuli. The same effect may also explain the latency changes in oVEMPs recorded when the eyes are closed (Huang et al., 2012). In contrast, with up- or down-gaze the oVEMP appears to be dominated by activity of the IO and IR muscles, respectively.

Our evidence supporting the importance of tonic muscle activity for the oVEMP implies that reflexes measured from the extraocular muscles show ‘automatic gain compensation’, whereby reflex amplitude and force output increase in parallel with tonic muscle contraction (Matthews, 1986). This mechanism causes the size of a reflex to remain constant relative to different levels of muscle activity, and is thought to be due to a change in the population of muscle units being available to change their firing rate in response to an external stimulus. This property is shared by other short-latency vestibular reflexes such as the cervical VEMP and vestibulo-spinal reflexes (Colebatch et al., 1994; Lim et al., 1995; Lee Son et al., 2008) and was earlier described for other proprioceptive reflexes, such as the stretch and H-reflexes (Capaday and Stein, 1987; Gottlieb and Agarwal, 1971; Matthews, 1986). Scaling with background contraction can be expected to occur whenever there is a consistent reflex effect on the motoneuron pool causing frequency modulation of discharge rate (Matthews, 1986). Unlike the cervical VEMP, it is not easy to measure the level of tonic activation of the IO using surface recordings. During fixation the discharge frequency of individual ocular motoneurons varies nearly linearly with gaze position, while the overall muscle force increases exponentially with increasing eccentric gaze angle (Davis-López de Carrizosa et al., 2011; Goldstein and Robinson, 1986). The findings of Govender et al. (2009) suggest that there is an approximately linear relationship between eye position and oVEMP amplitude up to at least 20° of gaze elevation. However it is not known whether the relationship between eye position and oVEMP amplitude is constant or whether it varies with changing task context.

Evidence in the literature concerning the presence of such a gain effect in the extraocular muscles is limited. Zhou et al. (2007) recorded click-evoked abducens nucleus activity and eye movements in monkeys at different horizontal gaze positions. They found a contralateral abducens excitation, which increased with increasing contralateral gaze (i.e. increasing lateral rectus activity). Results of these authors showed that the eye position effect was even greater than that expected for a simple linear relationship with tonic muscle activity and suggested a multiplicative interaction of vestibular and eye position signals. The animal model used by Zhou et al. is similar to our human experiment in terms of the short-duration otolith stimulus employed and provides support for the presence of automatic gain compensation in the extraocular muscles. In contrast, an earlier study by Cohen et al. (1966) investigated the extraocular muscle response to posterior semicircular canal nerve stimulation in cats and monkeys. They found no difference in the tension ratio between different extraocular muscles, but their main analysis came from the IR muscle during eye movements that were not in the pulling direction of this muscle.

There is also limited evidence concerning whether automatic gain compensation contributes to the changes in VOR direction or magnitude that may be seen with different gaze positions (e.g. Angelaki, 2004; Thurtell et al., 1999). Zhou and colleagues (2004, 2005, 2007) found that click-evoked eye movements and abducens activity in monkeys changed with different horizontal starting positions of the eye. Welgampola and colleagues (2009) found similar evidence in patients with superior canal dehiscence. They measured sound-evoked oVEMPs (i.e. IO muscle activity) and eye movements and found that the torsional component of the VOR and the IO muscle activity changed together. However, it is likely that these effects occurred because in each case only one ear was stimulated in isolation (by monaural sound stimulation) and therefore only one set of vestibular afferents was activated. In contrast, during normal head movements the drive to a pair of yoked eye muscles should be balanced due to differential activation of a pair of vestibular organs from opposite ears, which are jointly responsible for the reciprocal control of antagonist muscles (Cohen and Suzuki, 1963; Lorente de Nó, 1934; Szentagothai, 1950). Stimulation of vestibular afferents in a single ear would activate only half of the relevant VOR projections and the effects seen in one muscle would not be offset by those in its antagonist, leading to a change in the evoked eye movement. As such, we hypothesise that automatic gain compensation should not normally change the amplitude of vestibular evoked eye movements. For any eye position in the plane of an antagonist muscle pair (except neutral position), one muscle will have increased tonic activity and the other will have decreased activity (Björk and Kugelberg, 1953). Assuming relatively balanced reciprocal modulation of tonic activity at moderate gaze angles (Collins et al., 1975), when a transient eye movement is initiated from a non-neutral starting position, a larger muscle response in the tonically active muscle would automatically be offset by a smaller (and opposite polarity) response in its less-active pair. In this way an evoked eye movement should have approximately the same amplitude regardless of the starting point of the eye, as suggested by Welgampola et al. (2009). A recent study by Anagnostou et al. (2011) supported this hypothesis. The authors used natural, high-frequency horizontal head rotations (i.e. head impulses) and showed no change in the amplitude of the VOR evoked with different horizontal starting points of the eye. Our results are consistent with the proposal that, together with other mechanisms such as the normal elastic restoring forces of the orbit, (inverse) scaling of reflex modulation across antagonist muscle pairs contributes to vestibular-evoked eye movements remaining relatively constant across gaze positions.

Conclusion

We have shown that the effect of vertical gaze on the oVEMP is likely to be caused mainly by changes in tonic eye muscle activity. While the effect of muscle-electrode distance is also significant, it cannot alone account for the large effect of gaze on the oVEMP. Although surface electrodes will always reflect the summed activity of several extraocular muscles, the oVEMP is therefore likely to be dominated by responses of the closest tonically-active muscle to the recording electrode. Thus during up-gaze oVEMPs measured below the eyes originate in the IO, while during down-gaze they appear to be generated by IR activity.

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Figure Legends

Figure 1

Panel A. Experimental set-up, block 1. Angles used to test the effect of gaze: 24° elevation with 13° adduction, neutral (0°, i.e. aligned with the left eye) and 24° depression with 5° abduction. Panel B. Experimental set-up, block 2. Electrode positions used to test the effect of electrode-muscle distance. The superior edge of the upper recording electrode was aligned with one of the guide lines drawn underneath the eye and the lower recording electrode was placed directly below it on the cheek. The guidelines were drawn level with the inferior orbital margin (0 mm) and 2.4, 6.2, 10 and 20 mm below this point. Panel C. The dimensions of the IO muscle and its position in the orbit (see Appendix A). All values are in mm units. Panels D-F. The relationship between the IO and the surface electrode in the gaze neutral, up and down positions, respectively. The gaze up position is 24° elevation and 13° adduction and the gaze down position 24° depression with 5° abduction. Distances from the IO muscle to both the midpoint and superior edge of the electrode are shown. Panel G. Calculation of the electrode shift needed to simulate an IO muscle displacement relative to the midpoint of the electrode. A change in gaze from up (Panel E) to down (Panel F) produced a 2 mm difference in the closest distance from the IO muscle to the electrode midpoint (18.1 to 20.1 mm). To simulate this displacement the electrode should be moved 2.4 mm downward. Panel H. Calculation of the electrode shift required to simulate an IO displacement relative to the superior edge of the electrode. The up-to-down gaze shift produced a 3.7 mm difference in distance from the IO muscle to the superior electrode edge (11.4 to 15.1 mm). To simulate this displacement the electrode should be moved 6.2 mm downward. See Appendix A for more details.

Figure 2

Effect of gaze direction on the oVEMP. Panel A shows the grand mean response from the referential montage in 10 subjects in the gaze up, neutral and down conditions. The gaze up condition was 24° elevation with 13° adduction and the gaze down condition 24° depression with 5° abduction. There was a clear effect of gaze on the n10-p15 oVEMP: amplitude decreased as gaze was lowered to neutral position, and with down-gaze there was a delay in n10 latency. In neutral gaze the grand mean response appeared to consist of a combination of the gaze-up and gaze-down responses and both negative peaks could be identified in the neutral trace (the second marked with an asterisk *). Panel B compares the oVEMPs recorded with gaze up (black traces) and down (grey traces) using the referential electrode montage (overlay of up- and down-gaze from panel A). Panel C compares the same conditions recorded with the bipolar montage. The bipolar montage produced responses with the same morphology but smaller amplitude. In Figures 2 and 3: Stimulus artefact has been clipped for clarity.

Figure 3

Effect of electrode position on the oVEMP. The responses are the grand means from the referential montage in 10 subjects. Gaze was held constant in the up-gaze position and the oVEMPs were measured with electrodes at varying distances from the baseline position near the eye. As the electrodes were moved away from the eye the oVEMPs became smaller, but there was no change in n10 latency.

Figure 4

Reduction of oVEMP amplitude with increasing distance of recording electrode from baseline position. Here the electrode position is expressed in terms of the closest distance from the IO muscle. The relationship was best described by an exponential decay function.

Appendix A

The size of the IO and its spatial relationship to the orbit were estimated using anatomical data from several sources (Figure 1C). To determine the horizontal distance from the anterior edge of the IO muscle to the skin at the level of the inferior orbital margin, we first measured the axial length of the globe from Figure 1 in Demer et al. (2003) and compared this length to the average axial length of the globe of approximately 25 mm (González Blanco et al., 2008; Chang et al., 2001; Norman et al., 2010; Volkmann, 1869). We then measured the distance from the anterior edge of the IO muscle to the skin from the same Figure and calculated the actual value to be 12.5 mm based on the ratio found for axial length of the globe. To calculate the vertical distance from the muscle belly to the electrode, we compared data from several papers. The vertical distance from the inferior aspect of the globe to the orbital floor is about 7 mm (Darcy et al., 2008; Stephan et al., 2009). The IO muscle thickness at the point where it crosses the inferior rectus insertion is about 2.5 mm (Kaufmann and Steffen, 2004). We allowed 1.5 mm between the globe and the IO muscle to allow for the IR tendon (Kaufmann and Steffen, 2004). The distance from the inferior edge of the muscle to the floor of the orbit is 3 mm (i.e. 7 - 2.5 - 1.5 mm), therefore the distance from the middle of the IO muscle belly to the orbit floor is approximately 4.3 mm. The oVEMP electrodes have a diameter of 20 mm. We assumed that the superior edge of the electrode would be aligned with the floor of the orbit. The vertical distance of the IO muscle to the superior edge and midpoint of the electrode in neutral gaze is therefore approximately 4.3 and 14.3 mm, respectively. Based on the above values the distance from the anterior edge of the IO to the top and midpoint of the surface electrode is 13.2 and 19 mm, respectively (Figure 1D). Additional assumptions are that movement of the electrode downward on the face is approximately vertical and that signal conduction through periorbital tissue is similar in different directions and through different tissues. While the fat content of facial tissue is likely to increase with electrode distance, fat generally has low electrical conductivity. This would lead to smaller oVEMP amplitudes and would not negate our findings.

The anterior edge of the IO muscle has been shown to move 4.3 ± 0.3 mm anteriorly with a change of gaze from 24° depression with 5° abduction to 24° elevation with 13° adduction (Demer et al., 2003). Assuming that in neutral gaze the anterior muscle edge lies equidistant to these extremes, the muscle would move 2.15 mm forward from neutral position in elevation and backward in depression. Given a vertical height difference between the muscle centre and the middle of the recording electrode of 14.8 mm in elevation and 13.8 mm in depression, i.e. allowing for 1 mm vertical muscle movement (Demer and Clark, 2005), the distance from the anterior muscle edge to the electrode would be 18.1 mm in elevation (Figure 1E) and 20.1 mm in depression (Figure 1F). Thus there is a 2 mm difference in muscle-electrode distance when these two gaze positions are compared. To simulate this 2 mm change while keeping gaze constant in the elevated position, the electrode should be moved 2.4 mm downward (Figure 1G). If we instead base our calculation on the distance from the muscle to the superior edge of the electrode (a height difference of 3.8-4.8 mm), the distance from the muscle edge to the electrode would be 11.4 mm in elevation and 15.1 mm in depression (Figure 1E and F). To simulate this 3.7 mm difference, the electrode should be moved 6.2 mm downward (Figure 1H).